We have demonstrated[4] the antidystrophic action of d,l-alpha-tocopherol (synthetic vitamin E) in rabbits fed a diet containing lard and cod liver oil, and have emphasized the fact that the absence of physical symptoms does not exclude extensive microscopic muscle lesions.[5] Recently we have reported[6] that acute muscular dystrophy could be produced in the absence of cod liver oil or other animal fats in rabbits reared on a synthetic diet. The oral administration of 3 mg of alpha-tocopherol 6 days a week to rabbits on this diet afforded complete protection against muscle lesions. The preventive action of the vitamin E was counteracted by the oral administration of 1 cc of cod liver oil soon after the vitamin E.

In more recent experiments employing the same synthetic diet, we attempted to prevent the action of cod liver oil by administering 6 mg of alpha-tocopherol[7] orally on Mondays, Wednesdays and Fridays, and 2 cc of cod liver oil on Tuesdays, Thursdays and Saturdays. This procedure was employed by Shimotori, Emerson and Evans[8] in preventing dystrophy in guinea pigs on a synthetic diet. The rabbits supplemented in this manner developed lesions of the skeletal muscles equaling in severity those produced when the same levels of alpha-tocopherol and cod liver oil were administered within a few minutes of each other, three times a week. In both cases the lesions were frequently not accompanied by overt symptoms.

However, when the dosage of alpha-tocopherol was increased to 40 mg every other day, the administration of 2 cc of cod liver oil on alternate days was without effect. No microscopic lesions were detected in the skeletal muscles. Thus it is clear that alpha-tocopherol when administered in sufficient amounts and under the conditions described protects the rabbit against muscular dystrophy produced by the administration of cod liver oil.

The following propositions have now been demonstrated on rabbits receiving *the same basal ration:* (1) severe dystrophy develops in rabbits on a vitamin E deficient diet in the absence of cod liver oil; (2) alpha-tocopherol prevents this dystrophy; (3) cod liver oil counteracts the antidystrophic action of alpha-tocopherol and produces muscle lesions, (4) increasing the alpha-tocopherol sufficiently prevents the dystrophic action of cod liver oil. It seems probable that this quantitative relationship also applies to other species in which cod liver oil produces lesions of the skeletal muscles. A detailed report of these experiments will be published elsewhere.

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THE APPARENT EFFECT OF TYROTHRYCIN ON STREPTOCOCCUS HEMOLYTICUS IN THE RHINOPHARYNX OF CARRIERS

As yet no satisfactory method of eliminating pathogenic bacteria from the rhinopharynx of carriers has been devised. To this end a large number of chemical and physical agents have been unsuccessfully employed. Under the present conditions of shifting industrial populations and mobilization of troops, the problem again becomes urgent.

Dubos's recent isolation of a bactericidal substance from a soil bacillus ("tyrothrycin")[1, 2, 3] suggested that this agent might be effective in clearing the rhinopharynx of certain bacteria such as hemolytic streptococcus, meningococcus, pneumococcus and the diphtheria bacillus.

From cultures of *B. brevis* kindly furnished by Dr. Dubos, "tyrothrycin" was prepared according to the procedure which he has described.[3] The material was found to exert *in vitro* a lethal action on 18-hour broth cultures of hemolytic streptococcus, *staphylococcus aureus* and diphtheria bacillus (gravis strain) in a final dilution of 1:1,000,000, and on recently isolated strains of meningococcus (Type I) in a dilution of 1:100,000. The alcohol soluble fraction diluted 1:100 in normal saline containing 2.5 per cent. glycerine was introduced as a spray into the nose and throat of monkeys (*M. mulatta*) and of man. By means of copious spraying an attempt was made to cover as completely as possible the entire nasopharynx. This was often preceded by preliminary cleaning and shrinking of the mucous membranes. The active agent being insoluble in aqueous solution, vigorous shaking of the suspension was required immediately before use.

Separate nose and throat cultures from human beings were carried out for the demonstration of hemolytic streptococcus according to the method of Mueller.[4]

[4] C. G. Mackenzie and E. V. McCollum, *Jour. Nutrition,* 19: 345, 1940.
[5] C. G. Mackenzie, M. D. Levine and E. V. McCollum, *Jour. Nutrition,* 20: 399, 1940.
[6] C. G. Mackenzie, J. B. Mackenzie and E. V. McCollum, *Jour. Nutrition,* 21: 225, 1941.
[7] We are indebted to Merck and Company, Inc., for the supply of alpha-tocopherol.
[8] N. Shimotori, G. A. Emerson and H. M. Evans, *Jour. Nutrition,* 19: 547, 1940.

[1] R. J. Dubos, *Jour. Exp. Med.,* 70: 1, 1939.
[2] R. J. Dubos and R. Hotchkiss, *Jour. Biol. Chem.,* 136: 803, 1940.
[3] R. J. Dubos and R. Hotchkiss, *Jour. Exp. Med.,* 73: 629, 1941.
[4] J. H. Mueller and L. Whitman, *Jour. Bact.,* 21: 219, 1931.

Preliminary trials in two monkeys which were found to carry in the nasopharynx and throat gram positive hemolytic streptococci and gram negative hemolytic bacilli (*Hemophilus hemolyticus*?) suggested that both these bacterial species disappeared within 2 hours following the administration of tyrothrycin. Cultures taken 5 days after a single treatment revealed no hemolytic colonies in the case of one monkey, whereas in that of the other they appeared only in the throat cultures. Following a second application at this time all cultures were negative within 3 hours. Repeated cultures remained negative for at least 4 days without further treatment. No local or general reactions to the material either in these animals or in a human volunteer were observed.

Accordingly, 5 human carriers of hemolytic streptococcus were treated. Two of them had been persistent nasal carriers for two months following scarlet fever, and 3 were convalescent in the third week of this disease. The results are presented in Table I. Only

TABLE I

DATE OF CULTURE

Carrier		6/13		6/14		6/15		6/16		6/17		6/18		6/19		6/20	6/21	6/23
* L	N	+++		0		0		0		0		0		0		0	0	0
	T	0	S°	0	S	0	S	0	S	0	SS#	0	SS#	0	##	0	0	0
* McD	N	nd		nd		nd		++		+		+		0		0	0	0
	T	nd	S	nd	S	nd	S	++	S	+++	SS#	0	SS#	±	##	0	0	0
+ S	N	++++		++++		++++		++++		++++		±		++		++	0	0
	T	+++		++++	S	++++	S	++++	S	+++	SS#	±	SS#	0	##	0	0	0
+ McC	N	++++		+++		±		++		0		0		0		+	0	0
	T	+		+	S	+++	S	±	S	0	SS#	0	SS#	0	##	0	0	0
+ E	N	+++		++++		+++		++		+++		±		0		0	+	±
	T	0		++	S	++++	S	++	S	+++	SS#	±	SS#	0	##	+	0	0

*—Chronic carrier. +—Convalescent scarlet fever patient. ±—1 col. on plate; +—2–5 col. on plate; ++—5–10 col.; +++—many col.; ++++—pure culture with plate hemolysed. nd—Culture not received. S—Spraying. SS—Two sprayings. #—Preliminary cleansing before spray. ##—Spraying stopped at this time. °—Spraying preceded subsequent cultures by 16–24 hours at all times.

in the case of carrier L was an immediate reduction in the number of streptococci obtained. In the others it was not until the fifth day that a striking diminution or disappearance of the organisms occurred, although 3 to 4 sprayings had been administered. This abrupt change on the fifth day we ascribe to the more intensive application of the tyrothrycin begun at that time which seemed warranted by the entire absence of reactions from the smaller orienting doses. These preliminary observations are insufficient to indicate the value of tyrothrycin in the elimination of hemolytic streptococcus from carriers. They are sufficiently encouraging, however, to justify further trial of the material not only against this type of carrier but against others harboring diphtheria bacilli, meningococci and pneumococci. We are now investigating these possibilities.

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DEVELOPMENT OF HOMEOTHERMY IN BIRDS

ADULT birds are grouped with mammals as homeothermic or warm-blooded. The development of homeothermy occurs in the early life of the individual and corresponds to the increase in body temperature above that of the environment. This is accomplished through the appearance of special heat-regulating mechanisms presumably located in the base of the brain, in hypothalamus.[1]

Observations show that homeothermy in birds occurs either early or late in the development, depending largely upon the developmental state of the young at hatching. With altricious birds (pigeon, pelican), the young of which are naked and helpless for a while, the mechanism for the control of body temperature does not become effective until several days after hatching. Kendeigh and Baldwin[2, 3] showed on the house wren that the body temperature of a nestling rises above the external temperature primarily during the fourth to ninth days after hatching. On the other hand, with precocious birds (chick, turkey, pheasant) the young of which are covered with down and soon leave the nest, the mechanism for the control of body temperature becomes effective much earlier, presumably before hatching.

As to the time of the development of homeothermy

[1] S. W. Ranson, *Rev. Publ. Assn. Nerv. Ment. Dis.*, 20: 342–399, 1940.

[2] S. C. Kendeigh and S. P. Baldwin, *Am. Naturalist*, 62: 249–278, 1928.

[3] S. P. Baldwin and S. C. Kendeigh, Cleveland Mus. Nat. History, 3: 1–196, 1932.